



Trial Management Group Meeting # 19
26th April, Oxford

Draft Minutes

1. Those present

[Redacted]

[Redacted]

Observers

[Redacted]

2. Apologies

[Redacted]

[Redacted]

3. News

[Redacted]

ACTION 1: [Redacted]

[Redacted] has been successful in obtaining funding support for a PhD. The TMG congratulate [Redacted] on this achievement.

[Redacted] has been successful in obtaining an HSRC Fellowship grant and will be moving to [Redacted]

Thanks given to [Redacted] for the lunch voted best TMG lunch so far!

4. Agreement of agenda

All were happy with the agenda.

5. Previous minutes of TMG #18 and matters arising

The minutes of last meeting were accepted.

a) Financial contracts

Oxford contract has now been signed. The Royal Free hope to sign off the contract soon.

b) Centre Leader agreements

These are all signed, but the Royal Free contract has not yet been received (first copy lost in the post).

c) Red and Black screening books

This data is being stored electronically at Oxford.

d) SOPs

These have all been distributed. Further versions will be created and distributed as changes are requested.

e) Publication of the protocol

This is now at the final draft stage and we are just waiting for the last few people to give permission for their name to be published in the protocol.

f) The SCID

This has now been revised and distributed.

g) SSMC meetings

Concerns expressed that drop-outs are only from the SSMC alone arm. It is felt that some doctors are still not sure what advice they may give and are not confident about what is allowed within the remit of the trial protocol.

ACTION 2: [REDACTED] and [REDACTED] will run more meetings for SSMC doctors to support them in this and it is anticipated that this would take place in early June (possibly Monday 5th June 2006 for one at King's).

The team building the website are looking into the possibility of running a password protected forum or distribution list for staff.

h) DLA letters

Most centres are not writing DLA forms or insurance claim letters but others are. There is concern as to whether this could cause a centre effect if some centres but not others are involved in supporting these insurance claims. These letters were stopped at Bart's due to the time taken in writing these reports and a conflict of interests between supporting benefits and treating the illness. However, this centre sends out copies of clinical reports at a patient's request and with their permission. A second concern is that most clinics outside of PACE centres write these reports routinely. One service employs someone just to provide benefit advice and support. This might mean that PACE SSMC is not consistent with generalised SMC. The TMG agreed that clinics should continue with their normal practice, but consider writing reports on a case by case basis. The effect of benefits will be analysed at the end of the trial.

ACTION 3: The TMG agree that all centres should continue as per normal local practice regarding supporting DLA and insurance claims, and consider writing reports on a case by case basis.

i) Data Manager training

This will be run when all data managers are in post. In the meantime, the Royal Free Data Manager has had some training but now needs data to practise with.

ACTION 4: [REDACTED] to speak to the Royal Free about the Data Manager there to do the Oxford data entry whilst there is no data manager in post.

j) Double and increased recruitment for centres

[REDACTED] spoke to the reasons why King's do not feel ready to increase recruitment at this time. A high volume of referrals to this centre are unsuitable.

The TMG is now looking for centres to volunteer to be double or increased rate recruiting centres.

The TMG agreed that the reasons for blocks to recruitment need to be carefully analysed. It is thought that unsuitable referrals and doctor's time may be the greatest barrier.

ACTION 5: All centre leaders to analyse the reasons for blocks to recruitment at their centre and see what the possible solutions are. These reports should be sent to [REDACTED] by the end of May. If these relate to funding, the TMG may then decide to reallocate MRC funds designed for extra nurse time to other areas if this would resolve the problem.

ACTION 6: MREC permission to be sought for advertising the trial to GPs and other referring doctors (e.g. physicians).

ACTION 7: The TMG will also consider whether another centre should be identified to join PACE.

k) Participant newsletter

A suggestion was made that participants might be approached for contributions. An item on the advantages of taking part in a clinical trial was also suggested.

ACTION 8: Centre leaders should ask their therapists to identify any participants that might be suitable to write an article for the participants' newsletter.

l) [REDACTED]'s ancillary study proposal

The TMG supports this in principle but there remain concerns about the supervisors being both subjects and observers. The TMG do not want the person analysing the data to be a member of the trial team. There were concerns that the social health of the trial team might be affected by this methodology and that data might be biased by collection in this way. [REDACTED] spoke to the analysis of the data being run by MSc students. [REDACTED] has also suggested that the Edinburgh psychology team might also be able to carry this out.

ACTION 9: [REDACTED] to discuss with [REDACTED] the problem and possible solutions to the issue of subject as observer in the proposed therapy supervision ancillary study.

m) Edinburgh study

[REDACTED] is almost ready to submit this for funding to the ESRC. Ethical approval will be sought as a substantial amendment to PACE through West Midlands MREC.

ACTION 10: [REDACTED] and [REDACTED] to discuss with Edinburgh and QMUL about possible arrangements for sponsorship.

n) Genomics study

The MRC chose not to fund this study. The TMG were split on whether funding should be pursued for this research. The TMG were in agreement that further discussion with [REDACTED] on funding. The NIH call for funding might also be pursued.

ACTION 11: [REDACTED] to discuss further options with [REDACTED] of CDC for the genomics study.

p) Two year follow up study

This is being written up for submission and the DWP have indicated that they may be prepared to fund this. The TMG are in strong support of this proposal.

q) [REDACTED] qualitative study

This is in development.

r) Other research

The [REDACTED] at King's is interested in doing in a PhD and might be interested in looking at the moderators of change in therapy in the PACE trial.

s) Publication of the PACE trial manuals

Three issues were identified regarding the proposal that the treatment manuals should be published:

Firstly, the manuals are not stand alone guides and would not work without the supervision and training that has been given.

Secondly, the manuals need to be made available in their current form after the study so that the study could be replicated. In addition to this, supervisor's manuals will need to be written to accompany these manuals.

Thirdly, treatment leaders may wish to publish books on the therapies with additional and wider information but that these publications will be very different from the manuals used in PACE. The manuals were written to be discretely different from one another than those used in normal practice, Combinations of treatment might be used.

Discussion held that a supervisor's manual may need to be written for each therapy.

ACTION 12: [REDACTED] to invite treatment leaders to write a supervisor's guide regarding training and supervision to their manuals so that the study could be repeated.

Concern addressed that the SSMC manual had not been felt comprehensive enough to publish. This needs further discussion.

Proposal that all four supervisor's manuals be published in one volume with annotated notes.

Summary of decisions on publications of the manuals

No PACE manual should be published prior to the results being published. If treatment leaders want to write a self help guide or manual and publish this for a therapy, this could be done as long as no connection to PACE is inferred and no PACE copyrights are breached. Treatment leaders should be approached to write supervisor's manuals.

t) July meeting venue

The next TMG will be held at [REDACTED] as [REDACTED] is not available for the July meeting originally scheduled for [REDACTED].

ACTION 13: [REDACTED] to inform all members of the TMG that the next meeting will take place at [REDACTED].

u) Flexibility of 15 week session – Substantial Amendment

Permission is requested of the TMG to increase the booster session treatment window to be less rigid: If a booster session window is missed, every effort will still be made for the participant to still receive the booster session. The date of these delayed sessions will be recorded. The booster session should not take place during or after 50 weeks. The TMG agreed to this decision.

ACTION 14: ■ to make a Substantial Amendment to MREC to increase flexibility of the window of timing of the booster session. Every effort will be made to hold the booster session at 36 weeks. If it is not possible to hold it then, the session will be held as soon as mutually possible thereafter and no later than 49 weeks after randomisation.

ACTION 15: ■ to remind all teams that treatment schedule forms must be given to the RN/A at 52 weeks or at the end of treatment.

6. Recruitment

Congratulations to Edinburgh for increasing their recruitment rate. The trial as a whole is running at 76% target for recruitment, which is considered as satisfactory. The TMG will consider ways to increase recruitment at its next meeting after considering centre leaders' reports on blocks to recruitment and their solutions.

7. Second wave centres

a) Staff recruitment (therapists and research staff)

Data manager still missing from Oxford.

Research nurse/assistant still missing from the Royal Free. ■ from Bart's will cover this post in the interim.

Oxford have 33 patient names banked. 28 have been contacted, six have responded so far.

b) Therapist training

The CBT team have all been trained.

Two issues were raised:

Are all teams receiving supervision at the same frequency, and if not, will this bias the therapy quality between treatment arms?

The TMG thought not. CBT are having face-to-face supervision every six weeks. The Edinburgh therapist does not attend all of these. The GET and APT teams have face-to-face supervision quarterly, but also peer supervision separately.

It was agreed that supervision should be tailored to the needs of the team and the individual therapists. As long as competence judgements are ongoing and adherence to therapy by therapists is consistent, the frequency of supervision is not important.

ACTION 16: ■■■ to remind all treatment leaders that face-to-face supervision should be at least four times a year and more if felt necessary.

Peer supervision meetings are taking place but we have no available funding for this.

The TMG would support peer days but the cost to the trial must be minimal. In CBT, peer support is by phone and email but face-to-face supervision is more frequent. PI permission should be sought for costs given in advance of any of peer supervision days.

ACTION 17: ■■■ to inform treatment leaders of the decisions that:

a) Supervision should be tailored to the needs of the team and so may be more frequent than originally agreed if required; and

b) PIs and centre leaders to be included in planning training at places outside of London, and peer supervision days to ensure that costs can be covered.

c) Doctor training

ACTION 18: Training to be arranged for ■■■ by ■■■ or ■■■.

d) Research staff training

ACTION 19: Data management training to be arranged by ■■■.

Research Nurse/Assistant training will be given to the Royal Free staff member when recruited. All other staff were trained in March.

e) Participant recruitment

Oxford started in April, Barts II will start in May, the Royal Free start date will be determined by ethical approval being received.

f) Adjustment of TSC recruitment targets

ACTION 20: ■■■ to revise recruitment targets before the next TSC and DMEC meetings.

g) Randomisation for Bart's II therapists

Selection of therapists between the merged Bart's centre is a possible cause of selection bias. It has been decided that therapists should be chosen on availability of slots by the patient. The Research Nurse/Assistant will be reminded of the importance of not biasing this choice.

ACTION 21: [REDACTED] to be informed of the method for assigning therapists for the merged centres.

h) Digital recordings; theft of Dictaphone, importance of encryption and frequent downloading of recordings

The TMG wished to remind to all centres about the importance of storing DAR equipment and recordings securely. The digitally recorded data is as important as any other data that is being collected for the trial and it was underlined that we must be as mindful of the accurate collection and careful storage and back up of these recordings as we are of the data gathered on CRFs. SOP 14 details the information required for storing these recordings and [REDACTED] is in the process of revising the SOP to further clarify the frequency with which it is recommended that recordings are downloaded.

These procedures will be checked as part of routine monitoring and auditing visits.

ACTION 22: [REDACTED] to provide every centre with an encryption password for the digital recordings.

ACTION 23: All centre leaders to ensure that DARs are being handled according to the SOP.

ACTION 24: [REDACTED] to add digital recordings storage and transfer to the Monitoring Report.

8. First wave centre issues

- a) [REDACTED]
- b) [REDACTED]
- c) [REDACTED]

Other London therapists will be approached to temporarily cover the APT post. King's are considering training a CB therapist to deliver GET and may appoint a locum. We have three months notice for [REDACTED] which will hopefully be enough time to recruit another therapist.

ACTION 25: [REDACTED] to discuss options with [REDACTED] for training King's CBT therapists to give GET.

ACTION 26: ■ to ask ■ if ■ would be willing to temporarily cover APT at King's.

9. Actigraphy

■ has sent all actigraphy files that ■ has to ■ who will collate this to see if any are missing before the DMEC.

ACTION 27: ■ and ■ to meet to develop an actigraphy analysis strategy plan.

10. 52 week tests requiring SCID data (CDC, London etc.)

Psychiatric disorders at 52 weeks will not be assessed. We will analyse categorical presence/absence of CDC, London and Oxford criteria without these data.

11. Blood tests

Oxford cannot get T4 blood assays. This is only done if TSH is indicated. The TMG agreed that a TSH alone would be acceptable.

ACTION 28: ■ to modify the SOP to allow TSH only where T4 blood tests are not locally available, and to include this in the MREC Amendment.

■ reported that getting outstanding blood tests done by the Maudsley hospital had helped considerably.

12. Database issues

There have been issues with the database that have caused delays in rolling this out and have resulted in some data loss.

ACTION 29: All data managers to review data entered to ensure that none is missing in the latest version.

13. Preparations for DMEC

a) Definition of deterioration

A definition of deterioration has been written by the trial statisticians ■ and ■. ■ would like to discuss this at the next DMEC meeting. However, ■ needs a decision on this as it informs how the DMEC report will be written.

ACTION 30: ■■■ ■■ and ■■■ to clarify the definition of deterioration in further detail in advance of ■■■ compiling the DMEC report.

14. Homework compliance

A reminder that homework compliance should be reported to the Research Nurse/Assistant after every session.

ACTION 31: ■■■ to remind all teams that homework compliance must be reported Research Nurse/Assistant after every session.

15. Remaining blind to research data after 52 weeks

A reminder to all centres that no feedback from research sessions must be given to therapists or doctors from research staff.

ACTION 32: ■■■ to remind to all centres that no outcome feedback from research sessions should be given to therapists, doctors, or any member of the PACE team from research staff.

16. Budgets

The budgets are being worked up by QMUL finance and a clearer picture on expenditure is being developed.

ACTION 33: The PIs and ■■■ will meet to discuss the trial's overall financial situation.

17. Monitoring visits by ■■■ with PI and/or CL

Dates for monitoring visits are being arranged.

ACTION 34: ■■■ to arrange all first wave monitoring visits.

18. PACE team day – plans for the morning session

Suggestions are needed for the content for the morning session.

ACTION 35: All TMG to make suggestions for the PACE team day morning session.

19. Website

This is days away from being launched.

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